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Study to evaluate the effect of vitamin C supplement on pulmonary function test in COPDpatients.

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ABSTRACT

Introduction: A substantial body of evidence indicates that nutrition influences respiratory health. Much of the nutrition research has focused on the intake of fruits, vegetables, and antioxidant micronutrients, because lungs are subject to a wide range of oxidant induced insults and because antioxidant defenses play an important role in protecting the lungs from damage.

Materials and methods: Seventy five patients with COPD were included in the study. In their baseline clinical examination, malondialdehyde (MDA); red blood cell superoxide dismutase (SOD) and erythrocyte glutathione peroxides (GPx) levels were measured. All the above parameters were repeated after 12 weeks of supplementation with 1000 mg vitamin C daily.

Result: Serum MDA levels were significantly lowered, erythrocyte SOD and Gap activity were significantly higher after supplementation of vitamin C. No significant improvement in FEV1 and FEV1/FVC was observed after 12 weeks of vitamin C supplementation.

Conclusion: The present study shows that the plasma lipid peroxide (MDA) levels were decreased and antioxidants levels (GPx and SOD) increased after 12 weeks supplementation of vitamin C in patients with COPD. Exogenous supplementation with vitamin C does not have any significant effect on the spirometric measurements though it brings down the levels of MDA showing attenuation of further damage.

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Introduction

A substantial body of evidence indicates that nutrition influences respiratory health [1]. Much of the nutrition research has focused on the intake of fruits, vegetables, and antioxidant micronutrients, because lungs are subject to a wide range of oxidant insults and because antioxidant defenses play an important role in protecting the lungs from damage. A growing, but as yet inconsistent, body of evidence indicates that a low dietary intake of fruits and antioxidants, including vitamins A, C, and E, is associated with obstructive airway conditions and with deficits in adult lung function assessed by spirometric measurements of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) [2]. In recent population-based studies, decreased lung function was associated with low levels of antioxidant intake and serum levels of antioxidants. If causal, the associations of low antioxidant intake with adult lung function level may arise from a steeper decline of lung function during adulthood, reversible acute effects, and/or long-term effects of inadequate intake during the period of childhood growth and development. [3]

Few population-based studies have investigated the relation between intake of antioxidants and pulmonary function during childhood [4]. The existing evidence among children is consistent with the findings in adults, but it suggests that the assessment of the source of antioxidant intake may be important in defining the role of specific antioxidant vitamins, including vitamin C. In a cross-sectional study of 2,650 school-age children in England and Wales, the level of FEV1 was positively associated with the frequency of fresh fruit consumption and more weakly associated with green vegetables and salad consumption [5].

However, FEV1 was not associated with serum levels of vitamin C, suggesting that other micronutrients in fruit were important. Studies that consider dietary and total nutrient intake that include intake from food and vitamin supplements may be informative for determining whether consumption of the package of antioxidants in whole foods or of specific vitamins is important. Using the evidence available for adults and children, we hypothesized that a low intake of fruits, vegetables, and juices, as well as an inadequate daily total intake of antioxidant vitamins A, C, and E, is associated with deficits in childhood FVC, FEV1, and forced expiratory flow between 25 and 75 percent of forced vital capacity (FEF25–75) (22). The Children's Health Study offered an opportunity to investigate the role of inadequate dietary and total antioxidant vitamin, fruit, vegetable, and juice intake on children's lung function [6].

MATERIAL AND METHODS:

This is Open Label Randomized Prospective study also called 'Before and after' study carried out in the tertiary care centre. The study subjects were selected from pulmonary outpatient department.

Seventy five known patients with chronic obstructive lung disease with FEV1 < 80%, FEV1/FVC < 70% and age between 40 to 70 years of both sexes, with mean duration of disease 10 to 15 years were selected (n=75). Exclusion criteria were respiratory disorders other than COPD, malignancy, overt cardiac failure, recent surgery, severe endocrine, hepatic or renal diseases, and use of anticoagulant medication.

A detailed history, thorough general and systemic examinations were done. Age, body weight, standard height, body mass index (BMI) and blood pressure were measured. After written and informed consent, Tablet Limcee (500 mg bd) containing Vitamin-C or Ascorbic acid was given for twelve week to every patient. During the study period the treatment plan was not changed. They were instructed not to change their dietduring the study period. They were interviewed regarding any changes in lifestyle or abnormal events such as disease or infection at each examination. None of the patients used additional oral vitamins, either prior to or during the study period. After 12 weeks the investigations were performed. Under all aseptic condition, 12 hour fasting venous blood samples were collected from all participants in plain and fluoride bulbs.

All samples were taken in the morning to avoid the confounding effect of diurnal variation of oxidative stress parameters as reported previously. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for various parameters. The following investigations were done 'Before' and 'After' the supplementation of vitamin C. Pulmonary functiontests were evaluated with the use of body plethysmography. All pulmonary function testing was performed according to the European Respiratory Society standards with the patients in a sitting position by the same technician in order to ensure consistency of the technique. Three technically acceptable measurements were performed in each patient, and the highest value was included in the analyses. The calculations were performed using Udwadia's formula.

Blood for routine biochemical analyses, for the assessment of lipid peroxidation products, and for antioxidant enzymes were withdrawn by venepuncture under standardized conditions. Routine biochemical analyses were performed using standard techniques. Lipid peroxidation was assessed by measuring concentrations of thiobarbituric acid reactive substances (MDA) by spectrophotometry at 535 nm. Malondialdehyde (MDA) levels are expressed as nanomoles of thiobarbituric acid reactive substances formed per milliliter of plasma. Erythrocyte superoxide dismutase (SOD) levels were estimated based on the inhibition of pyrogallol autoxidation caused by SOD as described by Markland and modified by Nandi and Chatterji. Glutathione peroxidase (GPx) activities were determined in washed red blood cells obtained immediately after sampling from the whole blood anticoagulated with EDTA based on the methods described by Andersen.[7] All values are expressed as units per gram hemoglobin. After 12 weeks, spirometry and

measurement of MDA, SOD and GPx were repeated. The standard supportive treatment for COPD was continued in all the patients for 12 weeks. The outcome variables were: FEV1, FEV1/FVC, MDA levels, SOD levels and GPx levels. The statistical analyses were performed using t test, and P values < 0.05 were interpreted as statistically significant.

RESULTS:

Seventy five patients, 50 men and 25 women, were enrolled in this study. They were generally late middle-aged (mean age 54.8±1.7 years), with the average smoking history of 26.9±5.3 packyears. Twelve weeks supplementation of Vitamin-C (Tablet Limcee) 500 mg bddaily for 12 weeks produced reduction in mean MDA level (5.31±0.18 Vs 3.24±0.22; P < 0.001). SOD and GPx shows significant increase in mean level. SOD level (857.4±38.4 U/gHbVs 1142 ± 209 U/gHb, P < 0.05) and GPx (41.51±1.8 U/gHbVs 49.1±3.42 U/gHb; P < 0.05) levels were increased after 12 weeks of vitamin C supplementation. No significant improvement in FEV1 (1.35 ± 0.28 Vs 1.37 ± 0.16; P>0.05), FEV1/FVC (63.14 ± 1.22 Vs 64.26±1.47) were observed after 12 weeks of vitamin C supplementation. In this study, different parameters before and after supplementation of Vitamin-C (Tablet Limcee) 500 mg bddaily for 12 weeks were estimated and compared. For this parameter, the mean value and standard deviation (SD) were calculated in study group. 'Paired t test' was applied to test whether the differences in means were statistically significant or not. P-value less than 0.05 (P < 0.05) was considered to be statistically significant. P-value of less than 0.001 (P < 0.001) was considered to be statistically highly significant. The results of the present study are as follows.

DISCUSSION:

Our study indicates that a low intake of antioxidant vitamins may have adverse effects on pulmonary function in patients. We observed deficits in FVC, FEV1, and FEF25–75 among girls with the lowest levels of dietary and total intakes of vitamin C and among boys with a low intake of fruit juices that is frequently supplemented with vitamin C. [7]

Based on the lack of statistically significant dose-response relations between antioxidant vitamin intake and lung function level, our data raise the possibility that increased intake of antioxidant vitamins above the recommended daily allowance may not provide additional protection for lung function level. Our findings showing lung function deficits with inadequate intake of vitamin C are consistent with those of studies in adults showing that lower levels of FVC and FEV1 are associated with a lower intake of vitamin C, but they are inconsistent with the only reported investigation of the relation between vitamin C and lung function.[8] In the cross-sectional study of 50 subjects in England and Wales, Cook et al. reported that FEV1 was positively associated with the frequency of fresh fruits, green vegetables, and salad consumption but was not associated with serum vitamin C levels, suggesting a role for other nutrients in fruit. Several studies in adults have also reported the protective effects of fruit intake on lung function

or obstructive airway diseases. [9] The differences in findings in the Children's Health Study may reflect variation in diet habits among the populations or diet assessment methods.

In the study Health Study population, fruit juices, which were the leading contributor to vitamin C intake, were positively associated with lung function. Fresh fruit is also an important source of vitamin C, and the study population from the United Kingdom may have consumed more fresh fruits as a source of vitamin C than fruit juices during the period of the study; however, we could not assess this possibility because the consumption of fruit juices was not included in the published report by Cook et al. Additional information about fruit juice intake may contribute to understanding the differences between the studies. Cook et al. did not find an association between serum vitamin C levels and patients lung function. [9]

Although dietary assessment of vitamin intake using food frequency questionnaires is imprecise, the lack of association may also be the result of a mismatch between the time scale of the cross-sectional studies of lung function level that integrates growth over the life course and serum levels of vitamin C, which is a water-soluble vitamin with a relatively short half-life.[10] Short-term biomarkers, such as serum levels, may provide less accurate estimates of the average levels during childhood than those provided by questionnaire methods that characterize usual intake, such as the food frequency questionnaire method.

Several mechanisms for the protective effects of vitamin C on lung function have been investigated. Vitamin C is an important antioxidant in the extracellular respiratory lining fluid that protects proteases, antiproteases, epithelial, and immune cells from oxidant attack, and low levels may leave the lung relatively unprotected from oxidant stress. The importance of vitamin C to antioxidant defenses is illustrated by trials that document the protective effects of vitamin C supplementation on short-term changes in lung function in free-living subjects exposed to high levels of oxidant air pollutants. [11]

Vitamin C may contribute positively to lung health and reduce airway hyperreactivity, both of which are determinants of adult lung function.[12] Whether the association of flows with the antioxidant vitamins and juice intake results from enhancement of pulmonary function, protection against bronchospasm, or reduced airway hyperreactivity in subjects from the Children's Health Study is presently unknown because this analysis was cross-sectional and we cannot differentiate between acute and chronic deficits in lung function. Future longitudinal follow-up of the cohort may be informative about the acute and chronic effects on lung function growth and maximum attained lung function at maturity. [13-15]

CONCLUSION:

After supplementation of vitamin C 500 mg bd daily to COPD patients, serum MDA levels were significantly lowered, erythrocyte SOD and GPx activity were significantly

increased. No significant improvement in FEV1 and FEV1/FVC was observed after 12 weeks of Vitamins C Exogenous supplementation with vitamin C does not have any significant effect on the spirometric measurements though it brings down the levels of MDA showing attenuation of further damage. It is also likely that the different antioxidants differ in this overall association with the disease and with lung function. In conclusion, a 12 wk supplementation of standard treatment with Vitamins C daily, provided some clinical benefit although it augmented certain endogenous antioxidants.

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